

These amendments are believed to place the claims into condition for immediate allowance or into better condition for consideration on appeal, add no new matter and raise no issues that would require additional examination. Accordingly, entry of the foregoing amendments is respectfully requested.

## ***II. Status of the Claims***

Upon entry of the foregoing amendments, claims 26, 28, 33, 34, 37, 39, 40, and 117-135 are pending in the application, with claim 26 being the sole independent claim.

## ***III. Summary of the Office Action***

In the Office Action, the Examiner made three rejections of the claims. Applicants respectfully offer the following remarks to overcome or traverse each of these elements of the Office Action.

## ***IV. The Obviousness-Type Double-Patenting Rejection***

In the Office Action at pages 2-3, the Examiner has rejected claims 26, 28, 33-34, 37, 39-40 and 117-126 under the judicially created doctrine of obviousness-type double-patenting as being unpatentable over claims 190-191 of commonly owned U.S. Patent No. 6,603,608 (the '608 patent). Applicants respectfully disagree with the Examiner that claims 26, 28, 33-34, 37, 39-40 and 117-126 are not patentably distinct from claims 190-191 of the '603 patent. However, Applicants respectfully request that the Examiner hold this rejection in abeyance until identification of patentable subject matter in the present application, at which time Applicants will consider filing a terminal disclaimer.

**V. The Rejection Under 35 U.S.C. § 102(b) Over Soltis Is Traversed**

In the Office Action at pages 3-4, section 4, the Examiner has rejected claims 26, 28, 33, 40 and 117-126 under 35 U.S.C. § 102(b) as being anticipated by Soltis *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 85:3372 (1988). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:

Soltis *et al.* remain anticipatory to instant invention because although Soltis *et al.* do not disclose specific activities for their AMV-RT preparation, they clearly indicate the purification of their AMV-RT enzyme (see page 3374, second column) resulted in specific activities which were 10,000 to 100,000 times higher than those of alpha and beta subunits of ASLV RT. Considering that purified beta subunit of ASLV in table 1 indicates a specific activity of 2.7 units per milligram it is reasonable to deduce that activity of purified AMV-RT to be 2.7X 10,000 (or X 100,000) units per milligram which results in AMV-RT activities of 27,000-270,000 units per milligram which is within the range of RT specific activity (25,000-140,000 units/milligram) claimed here.

Office Action at page 3, section 4, line 10, through page 4, line 6. Applicants respectfully disagree with these contentions.

Claim 26 as amended (and hence claims 28, 33, 40 and 117-126 which depend therefrom) is drawn to a method of producing an ASLV reverse transcriptase having a specific activity of from about 30,000 units per milligram to about 140,000 units per milligram. Soltis *et al.* disclose a method of expression and isolation of the p95<sup>polβ</sup> and p63<sup>polα</sup> subunits of AMV-RT, and the specific activities thereof.

Soltis *et al.* state that the final isolated specific activities of p95<sup>polβ</sup> and p63<sup>polα</sup> are lower than the activity of purified AMV-RT by a factor of 10,000 to 100,000 (page 3374, column 2, lines 14-18). The specific activities of p95<sup>polβ</sup> and p63<sup>polα</sup> are 2.5 units/mg and 0.21 units/mg respectively (Table 1). The specific activity of the isolated AMV-RT was obviously known to

Soltis *et al.* at the time that the experiments involving p95<sup>polβ</sup> and p63<sup>polα</sup> were performed, and is therefore a discrete point in the analysis. Therefore, the logical interpretation of these data would be that the activity of p63<sup>polα</sup> (0.21 units/mg) is approximately 100,000 times lower than the activity of the isolated AMV-RT, and the activity of p95<sup>polβ</sup> (2.7 units/mg) is approximately 10,000 times lower than the activity of the isolated AMV-RT. It then follows that the activity of the isolated AMV-RT is between 21,000 and 27,000 units/mg. Moreover, the Examiner's analysis completely ignores the role of the p63<sup>polα</sup> activity in establishing the possible activity range of AMV RT, and assumes that the range is based only on the activity of p95<sup>polβ</sup>. It is clear that Soltis *et al.* are referring to the activities of both p95<sup>polβ</sup> and p63<sup>polα</sup> when they state that:

[T]he increases seen in specific activity probably do not correspond to a similar increase in purity of the p95<sup>polβ</sup> and p63<sup>polα</sup> proteins. Final specific activities are still lower by factors of 10,000 to 100,000 than that of purified AMV-RT, and protein analyses indicated that both p95<sup>polβ</sup> and p63<sup>polα</sup> were minor constituents in these preparations.

Soltis *et al.*, page 3374, column 2, lines 12-18 (emphasis added). The range referred to by the authors is obviously derived from the order of magnitude difference in activity between p95<sup>polβ</sup> and p63<sup>polα</sup>, as it relates to the discrete specific activity which the authors had previously determined. As such, even if the activity of Soltis *et al.*'s AMV-RT was 27,000 units/mg (the upper end of the possible range) it would not fall within the range specified in claim 26, as amended (about 30,000 - 140,000 units/mg). Thus, it is clear that Soltis *et al.* do not disclose the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully assert that Soltis *et al.* cannot and does not anticipate the invention as presently claimed. Reconsideration and withdrawal of

the rejection of claims 26, 28, 33, 40 and 117-126 under 35 U.S.C. § 102(b) over Soltis *et al.* are therefore respectfully requested.

**VI. The Rejection Under 35 U.S.C. § 102(b) Over Chernov Is Traversed**

In the Office Action at pages 4 and 5, section 5, the Examiner has rejected claims 26, 28, 34, 37, 39 and 117-126 under 35 U.S.C. § 102(b) as being anticipated by Chernov *et al.*, *Biomed. Sci.* 2:49 (1991) ("Chernov I"). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:

Chernov I in page 53 of their publication discloses that their RT (prepared by the same method as Chernov II) is purified to homogeneity. Considering that in previous publication namely Chernov II, said authors teach the specific activity of their preparation to be 20,700 units/milligram it is reasonable to assume that the RT preparation in Chernov I which was purified to homogeneity at least does have a specific activity of 20,700 units/milligram which is about 25000 units/milligram claimed instantly.

Office Action at page 5, lines 2-7. Applicants respectfully disagree with these contentions.

As noted above, claim 26 as amended is drawn to a method of producing an ASLV reverse transcriptase having a specific activity of from about 30,000 units per milligram to about 140,000 units per milligram. In contrast, Chernov I discloses methods for producing RSV RT, but does not disclose the specific activity of the enzymes produced by the methods disclosed therein. The Examiner relies on the activity of the enzyme preparation described in Chernov *et al.*, *Biokhimiya* 55: 586 (1990) (hereafter Chernov II), as support for this rejection.

The methods of the present invention produce ASLV reverse transcriptase that is between 45 % and 576 % more active than the enzyme isolated by the methods of Chernov I. Under no definition of the term "about" could such an increase in activity be disregarded as insignificant.

Further, the Examiner has provided no evidence or sound scientific reasoning to indicate that one of ordinary skill would consider an enzyme preparation that is at least 45% less active (*i.e.* the Chernov I preparation) to be "about" equal in activity to that produced by the presently claimed methods. Applicants respectfully submit that the activity of 20,700 units/mg disclosed in Chernov II, is not about 30,000 units/mg as claimed in the present invention.

Moreover, Applicants note that the Examiner only assumes that the activity of the enzyme preparations produced in Chernov I is greater than 20,700 units/mg because they have been "purified to homogeneity." There is absolutely no objective evidence in Chernov I to support such an assumption. Further, this assumption cannot even be said to be inherently supported in either Chernov I or Chernov II. There is no evidence in either of these references that purification to homogeneity results in the production of enzyme preparations that are necessarily higher in specific activity than the 20,700 units/mg reported in Chernov I. Indeed, as one of ordinary skill in protein chemistry would be well aware, purification of an enzyme to homogeneity frequently results in a *reduction* in enzyme activity due to aggregation, removal of a required cofactor or perturbation of the protein structure (and hence inactivation). Without any evidence either way, there is no reason to assume *a priori* that the enzyme preparations of Chernov I are necessarily more active than those of Chernov II.

As the Federal Circuit has held:

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

*Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1570 (Fed. Cir. 1988). Moreover:

Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.

*Continental Can Co. U.S.A., Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991) (emphasis added).

Since the Examiner has pointed to no express disclosure in Chernov I or Chernov II that sets forth enzyme preparations with the specific activities of those produced by the presently claimed methods, Chernov I does not expressly anticipate the claimed invention. Similarly, since the Examiner has not provided any basis in fact and/or sound scientific reasoning to support the assumption that an allegedly inherent specific activity higher than 20,700 units/mg *necessarily* flows from the disclosures of Chernov I and II, Chernov I does not inherently anticipate the claimed invention. *See Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. Int. 1990).

In view of the foregoing remarks, Applicants respectfully assert that Chernov I cannot and does not anticipate the invention as presently claimed. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

#### ***XIV. Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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